



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,448	06/04/2001	Patrick Midoux	USB98ASIDM	3117

466 7590 02/22/2007
YOUNG & THOMPSON
745 SOUTH 23RD STREET
2ND FLOOR
ARLINGTON, VA 22202

EXAMINER

SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
----------	--------------

1635

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/857,448

Applicant(s)

MIDOUX ET AL.

Examiner

Richard Schnizer, Ph. D.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25,26,28-34 and 36-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25, 26, 28-34, 36-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/18/06 has been entered.

Claims 25, 26, 28-34, and 36-41 remain pending and are under consideration in this Office Action.

All rejections from the previous Action which are not reiterated in this Action are withdrawn.

Claim Objections

Claims 25 is objected to because "p+q wherein" was added on page 4 of the response, but was not underlined to indicate this amendment. Claim 26 is objected to because "p+q" was added on page 8, but was not underlined. Applicant is reminded that 37 CFR 1.121 sets for the proper manner of making amendments to the claims, and requires the use of the proper status identifiers, and that the claims be marked up to show amendments. Failure to comply can result in issuance of a Notice of Non-responsive Amendment.

Claim 26 is objected to because it contains a chemical structure that is interrupted by a page break. The chemical structure at the bottom of page 26 is detached from the chemical structure at the top of page 27, and it is not possible to determine which atoms in these two structures are intended to be connected by a bond. Because no amendment to the structure is indicated, it is assumed for the purpose of examination that it is the same structure as set forth previously.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 25, 26, 28-34, and 36-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Midoux et al (WO 98/22610, published 5/28/98).

WO 98/22610 was filed as PCT/FR97/02022 and is the priority document for US Patent 6,372,499. The contents of WO 98/22610 will be discussed by reference to this English language version. Midoux teaches oligomers with a polymerization degree as low as 15, in which at least 10% of the monomers have free NH₃⁺ groups substituted by residues that are protonable in a weak acid medium, such as histidines, pterines, quinolines, or pyridines, leading to destabilization of cell membranes. See entire document, e.g. abstract; column 4, lines 20-24; column 4, line 55 to column 5, line 40; column 6, line 48 to column 8, line 43; and column 10, line 44 to column 11, line 38.

Art Unit: 1635

The R groups recited in the claims are set forth at e.g. column 10 line 44 to column 12 line 22, wherein $m = 1$, n is from 1-6, n' and n'' are both $= 0$, and B is an imidazole group. Instant R' is NH_3^+ .

It is noted that the instant claims require at least 50% substitution. However, the recited "at least 10%" in the cited art is reasonably interpreted as embracing 10% to 100%, so the instantly claimed "at least 50%" is embraced by the range in the cited art. As such it would have been obvious to one of ordinary skill in the art to arrive at the claimed conditions through the process of routine optimization within the range in the cited art. Note that the instant application shows that the instant invention functions to deliver polynucleotides when the level of substitution is 53%. See Table 1 on page 39.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 8/17/06 have been fully considered as they apply to the rejections set forth above, but they are not persuasive.

Applicant argues at pages 20 and 21 of the response that Midoux fails to teach selecting a degree of polymerization from 5 to 36, and a percentage of substitution greater than 50% such that the conjugates allow transfer of oligonucleotides into cells. This is unpersuasive. Midoux teaches oligomers with a polymerization degree as low as 15, in which at least 10% of the monomers have free NH_3^+ groups substituted by residues that are protonable in a weak acid medium, such as histidines, pterines, quinolines, or pyridines, leading to destabilization of cell membranes. The recited "at

Art Unit: 1635

least 10%" in the cited art is reasonably interpreted as embracing 10% to 100%, so the instantly claimed "at least 50%" is embraced by the range in the cited art. As such it would have been obvious to one of ordinary skill in the art to arrive at the claimed conditions through the process of routine optimization within the range in the cited art. Note that the instant application shows that the instant invention functions to deliver polynucleotides when the level of substitution is 53%, so this clearly would have been within the range of concentrations wherein it was reasonable and routine to optimize. See Table 1 on page 39. Therefore the invention as a whole was prima facie obvious. This polymer also allows the delivery of oligonucleotides, and so meets the new limitation "wherein said conjugate allows the transfer of oligonucleotides into a cell".

Applicant argues at pages 21 and 22 that instant Table 1 at page 39 presents evidence of unexpected results indicating the desirability of obtaining the claimed conjugates for use in transfection of cells with oligonucleotides. MPEP 716.02(b) states that evidence relied upon to establish unexpected results should establish that the differences in results are of both statistical and practical significance. There is no statistical analysis of the data in Table 1, so the standard for establishing unexpected results is not met. Note also that even if the results were of statistical and practical significance, they are not commensurate in scope with the claims. The results were obtained using histidylated oligolysine, whereas the instant claims are not limited to histidylated oligolysine but embrace a variety of backbones and any weak base. Furthermore it is not clear what is meant by the result "nd" for DNA results corresponding to 60, 80, and 100% histidylation. It could mean "not determined" or "not

Art Unit: 1635

detectable". However, because several results of "0" are reported (see under "ODN"), "nd" is taken to mean "not determined". As a result there is no data for plasmid DNA corresponding to these degrees of histidylation, so it is unknown whether or not these polymers would have functioned to provide transfection with plasmid DNA. Therefore it is not clear that the results observed with oligonucleotides are unexpected.

For these reasons the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Application/Control Number: 09/857,448

Page 7

Art Unit: 1635

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'R. Schnizer', with a long horizontal line extending to the right.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635